How E-cigarettes and vaping can affect asthma in children and adolescents

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Purpose of review
Electronic nicotine delivery systems such as e-cigarettes are commonly felt to be harmless devices when compared to traditional cigarettes. However, an increasing number of studies support the biological plausibility for the potential detrimental effects of vaping on the respiratory mucosa. To date, few human studies have been carried out on adult vapers showing a reduction in lung function testing, especially in those with asthma, whereas the effects of vaping on children and adolescents have not been elucidated so far.

Recent findings
Several cross-sectional, national, population-based studies on large groups of adolescents have been carried out showing an association between vape exposure and self-reported asthma diagnosis and/or respiratory symptoms in this age group. The effects of second and third-hand exposure together with those of active and passive exposure in pregnancy, are almost completely unknown.

Summary
This review outlines recent data on the potential effects of vaping on asthma, focusing on vape composition, reported effects on the respiratory mucosa, available data in adolescents, and reasons behind the current vaping epidemic. The evidence so far available both in animals and humans suggests that vaping is not harmless, and its exposure should be limited in children and adolescents, especially when affected by asthma.

Keywords
asthma, electronic cigarette, electronic nicotine delivery systems, smoking, vape

INTRODUCTION

The invention of electronic cigarettes (EC) dates to 1965 in the United States, when Herbert Gilbert patented the first model, which no company agreed to produce. In 2003, the Chinese pharmacist Hon Lik reinvented the device, proposing it on the Chinese market as a harmless alternative to traditional combustion cigarettes (CC) for the administration of nicotine. In 2006 and 2007, EC reached the European and American markets, respectively, achieving enormous success, with an exponential sales trend which is still in place today. EC and other electronic devices that deliver nicotine by simulating traditional smoking without tobacco combustion (electronic nicotine delivery systems [ENDS]) are commonly felt to be nonharmful solutions for smokers, considering that CC release more than 7000 compounds during combustion (at least 70 are known carcinogens) [1]. However, a growing number of scientific publications on the potential health effects of EC shows that these devices, although generally less harmful than CC, are not harmless, but rather represent a new source of danger, and not only for respiratory health [2▪▪,3▪].

Furthermore, these devices are enormously successful especially among adolescents, including those affected by asthma, and some studies have already shown how using ENDS represents the first step on the path that leads to becoming habitual CC

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KEY POINTS

- E-liquids and vape contain toxicants, but to what extent these are inhaled depends on many variables including vaping habits, e-liquid composition, the voltage of the device and the heat reached by the e-liquid.
- Experimental data and a few studies in adults show that vaping can exert negative effects on the respiratory system at multiple levels.
- Vape exposure is associated with self-reported asthma diagnosis and/or respiratory symptoms among adolescents and young adults.
- The use of electronic cigarettes is increasing among adolescents, mainly due to aggressive marketing strategies. Adolescents with asthma use electronic cigarettes more frequently than their healthy peers, due to the common misbelief that these devices are harmless.
- The long-term health consequences of vaping as well as of second and third-hand vape exposure are currently unknown and merit specific investigations.

smokers. Therefore, it is not surprising that many countries and local administrations are gradually introducing more stringent laws on the sale and marketing of these products and on vaping indoors.

Finally, it should be emphasized that, regarding the potential effectiveness of EC as a means of quitting smoking, the available evidence is conflicting, with some studies demonstrating their effectiveness [4,5] and others demonstrating that they may perpetuate addiction or even encourage dual-use [6].

This paper outlines recent data on the effect of vaping on pediatric asthma and the worrisome epidemic of ENDS use among adolescents, including those affected by asthma. For the purpose of this review, we will use the general term EC and we will not consider devices characterized by different aerosolization mechanisms such as pod-mods and heat-not-burn devices/heated tobacco products (HTP) (Table 1).

VAPE COMPOSITION AND POTENTIAL EFFECTS ON THE AIRWAYS

Generally, EC are made up of three main components: (1) a power source (usually a rechargeable lithium battery); (2) a heating element that vaporizes the solution (the atomizer), including a wick that absorbs the EC liquid (e-liquid) together with a metallic resistance that heats up when the electric current flows through it; (3) a liquid storage unit [7]. Since their introduction on the market, EC have undergone major structural and functional changes,

Table 1. Glossary

Cloud-chasing	Vaping technique with the goal to create different types of aerosol plume that is emerging as competition among teenagers.
Dabbing	The term comes from 'dabs', which indicates cannabis concentrates that can be aerosolized using ENDS.
Dripping	Vaping technique to inhale dense vapors not from the electronic cigarette mouthpiece but directly (the vapor is produced by manually dripping e-liquids onto the device's heating coils).
Dual user	User of both electronic cigarettes and traditional combustible cigarettes.
E-Cigarette	Electronic cigarettes are portable battery-powered electronic devices that simulate the act of smoking a traditional cigarette without burning tobacco.
ENDS	''Electronic Nicotine Delivery Systems' (ENDS) is a generic term used to identify all the available electronic devices used to deliver nicotine or nicotine-free liquids by inhalation.
EVALI	This acronym was introduced in 2019 and stands for 'E-cigarette or Vaping use-Associated Lung Injury'. EVALI is a diagnosis of exclusion in patients presenting with respiratory distress and a recent history of vaping or dabbing, abnormal chest CT, absence of signs of pulmonary infection or any other alternative plausible diagnoses.
Heat-not-burn devices/ Heated tobacco products	Electronic devices which generate aerosol by heating up tobacco without burning it.
JUUL	Pod-mod resembling a USB flash drive that delivers a high concentration of nicotine. The act of using the JUUL pod-mod device is known as 'juuling'.
Pod-mods	Miniaturized USB rechargeable vape devices.
Smoker	Combustible cigarette user.
Vape	The aerosol produced by ENDS, which usually appears denser than that produced by traditional cigarettes. The act of inhaling and exhaling the vapor produced by ENDS is known as 'vaping'
Vaper	Electronic cigarette user.

and the most recent models allow the user to customize the resistance and power, thus varying the temperature of the aerosol and, therefore, the sensation felt in the throat while vaping (a higher vape temperature gives the user a stronger 'throat hit') [7].

E-liquids consist of a solution mainly composed of a humectant such as propylene glycol (PG) or vegetable glycerine (VG) (85–90% of the solution), and one or more flavouring additives that give the vape a distinct aroma. Nicotine may or may not be included, with variable concentrations. More than 15,500 different flavours are currently available on the market, including food (fruit, sweets, candies) and drink (coffee, spirits) aromas. Unfortunately, several studies have shown that the description of the e-liquid ingredients does not always correspond to their real composition, so that, as an example, nicotine has been found in e-liquids declared as nicotine-free [8] together with other toxic compounds such as tobacco alkaloids, ethanol, formaldehyde and acrolein [9].

Moreover, despite being considered as safe food additives, PG and VG are hygroscopic molecules and thus their inhalation may cause the release of inflammation mediators in the airway mucosa. Interestingly, entertainment industry workers exposed to fog produced by heating VG and PG often complain of dry cough in the short term, whereas chronic exposure has been shown to cause chest tightness and wheezing, as well as lung function impairment [10]. Even EC flavouring additives are widely used in the food industry, but the inhalation of diacetyl (2,3-butanedione), commonly used to provide a 'buttery' or 'creamy/sweet' flavour, has been reported to cause bronchiolitis obliterans in factory workers involved in the production of microwave popcorn who are exposed to its aerosol ('popcorn worker's lung') [11,12]. Other flavours are well-known allergens (eugenol, clove aroma and cinnamaldehyde, cinnamon aroma) or irritants for eye and airway mucosa (benzaldehyde, fruity aromas) [13].

Furthermore, when e-liquids are heated to very high temperatures, the generated aerosol changes its composition with an increase in the concentrations of toxicants. When PG and VG are heated up to >215° C formaldehyde and acetaldehyde are released, whereas when VG is heated up to 270°C acrolein is produced too. All these compounds are cancerogenic or potentially cancerogenic and are known irritants for the airway mucosa [14]. Vape also contains other toxic agents such as ultra-fine particles, volatile organic compounds (e.g., benzene and toluene) [15], tobacco-specific nitrosamines and metals (such as iron, lead, nickel, chromium) [1], even if in smaller amounts when compared to CC. What exactly vapers inhale is hard to tell, since empirical studies are based on vape obtained under standardised conditions whereas vapers' exposure depends on a wide range of variables including vaping habits, e-liquid composition, the voltage of the device and the heat reached by the e-liquid [16].

Table 2. Main effects of vaping on the airway mucosa documented both in vitro and in vivo

• Recruitment of immune cells to the site of exposure
• Impaired ciliary beating
• Impaired macrophage and neutrophil function
• Altered host-defence gene expression
• Direct cytoxicity
• Decreased cough reflex sensitivity
• Promotion of protease-mediated lung tissue damage
• Altered cystic fibrosis transmembrane conductance regulator functioning, with increased mucus viscosity
• Increased airway hyperreactivity, airflow resistance, pro-inflammatory cytokine secretion, oxidative stress

Unsurprisingly, many studies, both in vitro and in animal models, have shown that vaping determines cytotoxic effects, oxidative stress, pro-inflammatory cytokines production and host defence impairment (Table 2) [17]. Recent evidence on adult vapers confirms these experimental observations and shows that vaping can exert negative effects on the respiratory system at multiple levels [18].

Vaping also exerts acute effects on lung function, resulting in increased respiratory flow resistance, overall peripheral airway resistance and reduced fractional exhaled nitrogen oxide (FeNO) both in smokers [19] and in never smokers [20]. A reduction in lung function testing as assessed by spirometry has also been reported [21,22]. EC may also cause a severe acute lung injury now known as E-cigarette or Vaping use-Associated Lung Injury (EVALI). This condition was first described in 2019 in the United States (US) in adolescents and young adults vaping e-liquids containing tetrahydrocannabinol and vitamin E acetate, who presented with severe respiratory distress together with ground-glass opacities in both lungs and dense consolidation in a peribronchial and perilobular distribution, with relative subpleural sparing at the chest CT scan, compatible with chemical pneumonia [23▪▪,24▪▪]. Variable gastrointestinal and constitutional symptoms may also be present [25,26▪▪], which seem more common in adolescents than in adults [27▪▪,28▪].

Finally, the long-term consequences of vaping are unknown and only limited data are available in animal models [29]. The presence of known

cancerogenic compounds in vape suggests caution and warrants specific investigations [30▪]. The effects of second and third-hand EC smoke exposure are not well known either, even if there are some reports on acute ocular, nasal, and pharyngeal irritation in adults exposed to second-hand smoke, together with increased levels of ultrafine particle, nicotine, volatile organic compounds in the indoor air of vapers' houses [31,32▪,33]. The consequences of vaping in pregnancy are unknown, but it should at least be considered that nicotine delivered by EC may interfere with fetal lung development, as it occurs with CC.

POTENTIAL EFFECTS OF VAPING IN ASTHMA

Asthma is the most common chronic disease in childhood [34] and its onset and poor control have been linked to multiple factors including active and/or passive tobacco smoke exposure in both adults and children [35–37]. Despite the spread of ENDS use, data on its effects on asthma are limited, mainly due to the heterogeneity of devices, e-liquids, and smoking habits. However, it is expected that vaping may be detrimental to these patients due to its proinflammatory and bronchoconstriction effects [38▪▪]. Some studies performed on adults with asthma confirmed such hypothesis. Lappas *et al.* have shown that even a single EC session can cause immediate inflammation and bronchoconstriction on peripheral and central airways as assessed by impulse oscillometry and FeNO, both in healthy and asthmatic adult smokers [39]. Similar results have been reported by Kotoulas *et al.*, who have found a worsening in spirometry and oscillometry parameters, together with changes in airway inflammation markers, in a small group of adults with moderate and stable asthma, 15 min after having vaped the same EC for 5 min [40▪]. Moreover, population-based studies have shown a longitudinal association between former or current EC use and respiratory diseases, including asthma and chronic obstructive pulmonary disease (COPD), after adjusting the results for CC smoking, demographic, and clinical variables [41▪▪], with worse effects for daily use as compared to occasional use [42]. Notably, vaping is more popular among adolescents with asthma as compared to their nonasthmatic peers and this is likely to be due to the belief that vaping is safer than CC [43]. Nevertheless, there is still a paucity of data on the effects of vaping in children and adolescents with asthma, with most of the available evidence coming from epidemiological studies on self-reported respiratory symptoms such as cough and phlegm or self-reported diagnosis of asthma by a physician in the previous 12 months (Table 3). In a recent systematic review and meta-analysis, the authors evaluated all the available studies up to March 2020 on the association between EC use with COPD and asthma, including both adults and adolescents, and showed a significant association with both conditions (15 studies on asthma, adjusted odds ratio (aOR) 1.39 [95% CI, 1.28–1.51]; 9 studies on COPD, aOR 1.49 [95% CI, 1.36–1.65]). Among the 15 selected studies on asthma, 11 included adolescents and were typically school-based data collections, mainly on high school students [44▪▪], of which 6 were carried out in the US [43,45–49], 4 in Asia [50–53] and 1 in Canada [54]. Taken together, these studies show increased odds of self-reported diagnosis of asthma by a physician and current asthma in the previous 12 months in current EC users compared with never users, as well as increased odds of reporting chronic cough or phlegm, and/or bronchitis, and school absences due to asthma symptoms.

A few other similar studies have been published more recently. Tackett *et al.* evaluated the association between self-reported wheezing in the previous 12 months and EC use in 7049 adolescents without asthma in a nationally representative cohort survey held in the US, showing an increased odds ratio of wheezing in those who had used EC in the previous year (OR 1.74; 95% CI, 1.22–2.48). Notably, in the adjusted model, after controlling for the variables of ethnicity, household second-hand smoke exposure, contact with a smoker in the previous 7 days, and use of combustible tobacco products, the association was no longer significant, suggesting that other risk factors may be associated with the development of wheezing in adolescents [55▪]. Alnajem *et al.* conducted a school-based cross-sectional study including 1565 high school students (aged 16–19 years) in Kuwait, investigating, through a self-completed questionnaire, tobacco product use, household second-hand exposure to EC and asthma symptoms (current wheeze, current asthma, and current symptoms of uncontrolled asthma). The study shows that current (any use in the previous 30 days) EC users with no history of CC use had an increased prevalence of current wheeze (adjusted prevalence ratio (aPR) 1.54; [95% CI, 1.01–2.45]) and current asthma (aPR 1.85; 95% CI, 1.03–3.41). Frequent household secondhand aerosols from EC was associated with current wheeze (aPR 1.30; 95% CI, 1.04–1.59), current asthma (aPR 1.56; 95% CI, 1.13–2.16), and current uncontrolled asthma symptoms (aPR 1.88; 95% CI, 1.35–2.62) [56▪]. Chung *et al.* used the data from a large survey carried out in 2018 on 60.040 Korean middle and high school students aged 13–18 years to evaluate the

Table 3. The table summarizes the available data on the effects of EC on asthma and/or respiratory symptoms in adolescents. Notably, all these studies are cross-sectional surveys

First author	Year of publication	Country	Number of subjects	Age	ENDS use	Outcome	Results	Adjusted odds ratios
Cho ref. [50]	2016	Korea	35.904	Mean: 16.4 ± 0.9 years	Current EC users (in the previous 30 days), former EC users, never EC users	Self-reported doctor diagnosis of asthma in the previous 12 months and school absences due to asthma symptoms	EC user is associated with asthma diagnosis and more days of absence from school due to severe asthma symptoms	aOR for asthma in current EC and never CC users: 2.74 (95% CI: 1.30–5.78).
Wang ref. [53]	2016	Hong Kong (China)	45.128	Mean: 14.6 ± 1.9 years	Never users, experimental users (smoked once or a few times), former users, current users (in the previous 30 days).	Self-reported respiratory symptoms (cough or phlegm) for 3 consecutive months in the previous 12 months	EC use is associated with respiratory symptoms in never- and ever-smoking adolescents	aOR for respiratory symptoms in current EC and never CC users: 2.06 (95% CI: 1.24–3.42)
Choi ref. [45]	2016	Florida (US)	36.085	Mean: 16.08 ± 0.02 years	Current EC users (in the previous 30 days), ever users, never EC users	Self-reported asthma status (never diagnosed, current asthma, no current asthma, unsure about current asthma status) and asthma attacks during the previous 12 months	Current EC use was associated with having current asthma and having an asthma attack in the previous 12 months among participants with asthma	aOR for current asthma in asthmatic current EC users: 2.20 (95% CI: 1.47–3.31)
Fedele ref. [46]	2016	Florida (US)	32.921	Range: 14–18 years	Current EC users (in the previous 30 days)	Self-reported doctor or nurse diagnosis of asthma and current asthma	Students diagnosed with asthma reported significantly higher current EC use than students without asthma	aOR for current asthma in asthmatic current EC users: 1.34 (95% CI: 1.15–1.57)
Larsen ref. [54]	2016	Ontario (Canada)	2.840	Mean: 15.9 ± 1.3 years	Ever EC users in the last 12 months, never EC uses	Self-reported use of cigarettes, waterpipes, marijuana or e-cigarettes.	Adolescents with asthma have higher odds of smoking EC than those without asthma	aOR for EC use in the previous year in patients with asthma: 1.78 (95% CI: 1.15–2.76)
Schweitzer ref. [43]	2017	Hawaii (US)	6.089	Mean: 15.8 ± 1.3 years	Ever EC use; current EC use (in the previous 30 days)	Self-reported doctor or nurse diagnosis of asthma and current asthma	Current EC use was associated with currently having (vs. never having) asthma	aOR for current asthma in current EC users: 1.48 (95% CI 1.26–1.74)
McConnell ref. [49]	2017	California (US)	2.086	Mean: 17.3 ± 0.6 years	Current EC users (in the previous 30 days), former EC users, never EC users	Self-reported chronic bronchitic symptoms (daily cough for 3 months, phlegm, or bronchitis) and of wheeze in the previous 12 months	Adolescent EC users have increased rates of chronic bronchitic symptoms.	aOR for bronchitic symptoms in former EC users: 1.71 (95% CI, 1.20–2.43) aOR for bronchitic symptoms in former EC users, never CC users: 1.70 (95% CI, 1.11–2.59)
Kim ref. [51]	2017	Korea	216.056	Range: 12–18 years	Current EC users (in the previous 30 days)	Self-reported doctor diagnosis of asthma in the previous 12 months or ever.	Current EC use was associated with asthma in the previous year.	aOR for asthma in the previous year in current EC users: 1.13 (95% CI, 1.01–1.26)
Lee ref. [52]	2019	Korea	58.336	Mean: 15.0 ± 1.8 years	Ever use of CC, EC and/or HTP	Self-reported doctor diagnosis of asthma or allergic rhinitis or atopic dermatitis in the previous 12 months.	Triple use of these tobacco products was associated with a higher risk of asthma, allergic rhinitis or atopic dermatitis. Sole use of HTP was strongly associated with asthma.	aOR for asthma in the previous year in ever EC only users: 1.23 (95% CI, 1.00–1.52) aOR for asthma in the previous year in ever HTP only users: 3.59 (95% CI, 1.47–8.78)
Bayly ref. [47]	2019	Florida (US)	11.830 with self-reported diagnosis of asthma	Range: 11–17 years	Exposure to aerosols from ENDS in the previous 30 days (at home, in cars)	Self-reported asthma attack in the previous 12 months	Second-hand ENDS aerosol exposure was associated with higher odds of reporting an asthma attack in the previous 12 months	aOR for asthma attack in second-hand exposed subjects: 1.27 (95% CI, 1.11–1.47)

Table 3 (*Continued*)

First author	Year of publication	Country	Number of subjects	Age	ENDS use	Outcome	Results	Adjusted odds ratios
Wills ref. [48]	2020	United States	14.765	Range: 14–18 years	Current EC users (in the previous 30 days), ever users	Self-reported doctor diagnosis of asthma	A significant association with asthma was found for current and ever use of EC	aOR for asthma in the previous year in current EC users: 1.30 (95% CI, 1.10–1.53) aOR for asthma in the previous year in ever EC users: 1.15 (95% CI, 1.02–1.30)
Tackett ref. [55▪]	2020	United States	7.049	Range: 12–17 years	Never users, no use in the previous 12 months, current EC users (in the previous 30 days), use in the previous 7 days	Self-reported episodes of wheezing in the previous 12 months	A significant association with wheezing was found only in the unadjusted model for EC users.	aOR for wheezing in the previous year in current EC users 1.35 (95% CI, 0.63–2.88); in EC use in the previous year 1.37 (95% CI, 0.91–2.05); in EC use in the previous 7 days 0.74 (95% CI, 0.28–1.97)
Alnajem ref. [56▪]	2020	Kuwait	1.565	Range: 16–19 years	Current EC users (in the previous 30 days), second-hand exposure to EC in the past 7 days)	Self-reported current wheeze (previous 12 months), current asthma (history of clinical diagnosis and current wheeze and/or medication use), and current symptoms of uncontrolled asthma	E-cigarette use and their household SHA exposure were independently associated with asthma symptoms among adolescents	aOR for current wheeze in the previous year in current EC users: 1.54 (95% CI, 1.01–2.45) aOR for current asthma in current EC users: 1.85 (95% CI, 1.03–3.41)
Chung ref. [57▪]	2020	Korea	60.040	Mean: 15.2 ± 0.02 years	Current users (in the previous 30 days), former (not within the previous 30 days) or never user of CC, EC and HTP	Self-reported doctor diagnosis of asthma and/or allergic rhinitis in the previous 12 months	Current sole EC use was associate with current AR but not with asthma; higher risk of asthma and AR compared with current CC only users in those using CC + EC and/or HTP.	aOR for asthma in the previous year in current EC only users: 1.00 (95% CI, 0.4–2.2)
Cherian ref. [58▪]	2021	United States	9.750	Range: 12–17 years	Use of ENDS in the previous 12 months	Self-reported wheezing in the previous 12 months; doctor or nurse diagnosis of asthma in the previous 12 months	No association between asthma diagnosis and ENDS use. ENDS use was associated with wheezing and dry cough in the previous year.	aOR for wheezing in general in ENDS users 1.37 (95% CI, 1.11–1.71); wheezing 4–12 times per year 1.57 (95% CI, 1.01–2.46); wheezing > 12 times per year 2.58 (95% CI, 1.04–6.41) aOR for dry cough at night in ENDS users: 1.23 (95% CI, 1.04–1.46)

aOR, adjusted odds ratio; aPR, adjusted prevalence ratio; EC, electronic cigarettes; CC, combustion cigarettes; ENDS, electronic nicotine delivery systems; HTP, heated tobacco products.

relationship between current asthma and/or allergic rhinitis and novel tobacco product user status. This showed an increased risk of allergic rhinitis and asthma in patients using both CC and EC and/or HTP when compared with current CC-only users. Such risk was not increased in those using EC or HTP alone [57▪]. Finally, in a nationally representative study among youth in the US including 9750 adolescents aged 12–17 years, Cherian *et al.* showed that, compared to nonusers, the previous year EC users had 37% higher odds of wheezing in general (aOR 1.37; 95% CI, 1.11–1.71, $P = 0.005$) and higher odds of wheezing 4–12 times or >12 times per year (aOR 1.57; 95% CI, 1.01–2.46, $P = 0.05$ and aOR 2.58; 95% CI, 1.04–6.41, $P = 0.04$, respectively). Moreover, they had 23% higher odds of dry cough at night compared to nonusers (aOR 1.23; 95% CI, 1.04–1.46, $P = 0.02$) [58▪].

Overall, it should be noted that all these studies are limited by their observational design, which does neither allow the evaluation of a causality relationship between respiratory symptoms/asthma and vaping, nor whether respiratory symptoms are secondary to airway inflammation and/or to increased susceptibility to infections. Notably, to our knowledge, no data is currently available on the respiratory effects of vaping in children (age < 12 years).

VAPING: A NEW EPIDEMIC AMONG ADOLESCENTS

The use of ENDS is increasing worldwide, especially among young adults and adolescents, mainly due to aggressive marketing strategies. Data from the National Youth Tobacco Survey shows that in the US in 2020, 19.6% of high school students and 4.7% of middle school students used an EC in the 30 days prior to the interview [59,60]. Similar data are available for other countries [50,61–63]. Adolescents are more likely to develop nicotine addiction than adults because the neural circuits underlying the curiosity to try new experiences develop faster than the circuits involving impulse control and decision-making. Moreover, their brain is more sensitive to the pharmacological properties of nicotine, so that the earlier they begin smoking, the less likely they are to stop using tobacco products [64,65]. It has been reported that vaping is associated with an increased risk of also becoming users of CC (the so-called 'gateway' effect), with the result that adolescents who have never used CC, but have tried EC at least once, have a 3–4 times greater risk of starting smoking CC [66]. Therefore, it is not surprising that young people are the main target of advertising campaigns by EC brands, most of which are owned by tobacco companies: children and adolescents are the target population to replace current smokers who will either die prematurely from smoking or who will quit smoking [67].

The main strategy to appeal to younger people is advertising the most up-to-date technology to deliver nicotine together with many flavouring options [63]. Although the sale of flavoured CC has been banned for years, restrictions on the possibility to flavour EC liquids are scant, leaving the industry free to take advantage of this crucial factor in attracting young people to use [68▪]. Moreover, thanks to fruity, candy or menthol flavours, there is a reduction in the taste of bitterness that would be experienced with the use of nicotine alone, allowing more vaping and strengthening the perception by adolescents that EC is less harmful than it really is.

Packaging is also designed to appeal to children and adolescents, making the products look like candy or juice boxes [67]. As a whole, EC is proposed as a healthier, cheaper and cleaner alternative to CC and the message is so well delivered that many adolescents are not even aware that EC can contain nicotine [69,70▪▪]. In addition, there is wide availability of these products online and in specialized stores, with little or no restrictions on sale [63,68▪]. Pod-mods, new devices resembling USB flash drives, are undergoing great success among young people because of their modern design that can be disguised, allowing students to vape in school bathrooms or even in the classroom. Such devices are particularly dangerous since their nicotine formula is derived from nicotine salts which deliver a higher concentration to the user with minor irritation to the airways [71,72▪]. Teenagers currently consider vaping as 'cool', making them feel more socially accepted and 'in-trend'. Many websites show the different ways of using ENDS: for example, the 'dripping' technique consists in dropping the EC liquid onto the heating coil to directly inhale the vapour, which will be denser and richer in nicotine, whereas 'cloud-chasing', allows creating clouds of vapour, transforming the use of EC into a fun game to be shared with friends or even in real competitions [73▪▪]. Therefore, driven by curiosity to try their favourite flavour, supported by their peers who already use them, and unaware of the potential risks and consequences for their health, adolescents can easily approach the use of ENDS. Moreover, drugs such as marijuana, methamphetamine and other stimulant substances may be added to e-liquids, which has contributed to increasing the popularity of these devices among young people [74].

CONCLUSION

The use of ENDS is increasing worldwide, especially among young adults and adolescents, due to

aggressive marketing, as well as the false belief in their safety. However, evidence is growing on their potentially detrimental effects on the airways in the short and likely in the long term. Adolescents and children with asthma are particularly at risk. In these age groups data are limited to population-based studies showing increased odds of self-reported respiratory symptoms. More studies are urgently needed to shed light on vaping exposure-related health risks. In the meantime, healthcare professionals should educate their young patients and their families on the potential consequences of smoking and vaping in order to prevent initiation. They should also identify patients who are current smokers to provide support in treating addiction and consider screening with specific questions on EC use all patients with recurrent respiratory symptoms of unknown origin or uncontrolled asthma. Finally, it is advisable that governmental bodies strengthen measures aimed at reducing and discouraging the use of ENDS among young people.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

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